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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,228	04/12/2001	Elaine L. Jacobson	NIAD-214.1 US	3352

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[REDACTED]  
EXAMINER

HUI, SAN MING R

ART UNIT	PAPER NUMBER
1617	[REDACTED]

DATE MAILED: 01/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/834,228	JACOBSON ET AL.	
	Examiner San-ming Hui	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on \_\_\_\_.  
 2a) This action is FINAL.                  2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-16 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_ is/are allowed.  
 6) Claim(s) 1-16 is/are rejected.  
 7) Claim(s) \_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 11) The proposed drawing correction filed on \_\_\_\_ is: a) approved b) disapproved by the Examiner.  
     If approved, corrected drawings are required in reply to this Office action.  
 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All b) Some \* c) None of:  
     1. Certified copies of the priority documents have been received.  
     2. Certified copies of the priority documents have been received in Application No. \_\_\_\_.  
     3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
     \* See the attached detailed Office action for a list of the certified copies not received.  
 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
     a) The translation of the foreign language provisional application has been received.  
 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                   | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)          | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ . | 6) <input type="checkbox"/> Other: _____                                    |

## DETAILED ACTION

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, and 9-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for C<sub>1</sub>-C<sub>18</sub> ester of niacin, does not reasonably provide enablement for other derivatives of vasodilator compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In the instant case, the specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence or absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art

- 7) the predictability of the art, and
- 8) the breadth of the claims.

Applicant fails to set forth the criteria that defines "derivative of a vasodilator compound". Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "derivative of a vasodilator compound" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The instant claims read on all "derivative of a vasodilator compound", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, and 9-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "derivative of a vasodilator compound" in claim 1, line 2 renders the claims indefinite as to the compounds encompassed thereby.

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The term "log P" in claim 1 renders the claims indefinite because it is unclear what the term "log P" refers to. Is it the log value of the partition coefficient between water and octanol or is it the log value of the partition coefficient between water and other organic solvent?

The expression "about 1 to about 12 carbon atoms in an alkyl chain" in claim 5 renders the claim indefinite as to the number of the carbon in the compounds. The number of carbon in an alkyl chain can be whole number only. Therefore it is unclear what compounds are encompassed by the claims.

The expression "about 6 to about 12 carbon atoms in an alkyl chain" in claims 6 and 9 renders the claim indefinite as to the number of the carbon in the compounds. The number of carbon in an alkyl chain can be whole number only. Therefore it is unclear what compounds are encompassed by the claims.

The expression "about 8 to about 10 carbon atoms in an alkyl chain" in claims 7 and 10 renders the claim indefinite as to the number of the carbon in the compounds. The number of carbon in an alkyl chain can be whole number only. Therefore it is unclear what compounds are encompassed by the claims.

Claim 16 recites the limitation "said ester" in line 1. There is insufficient antecedent basis for this limitation in the claim.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3-5, 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rine (US Patent 5,738,879) in view of Le et al. (International Journal of Pharmaceutics, 1998; 163: 11-22) and Otsuka et al. (US Patent 5,151,271).

Rine teaches a method of hair treatment by applying a shampoo composition comprising a vasodilator ethyl nicotinate, a C<sub>2</sub> ester of niacin, in the weight percentage of 0.10-0.50% (See particularly the abstract, col. 1, line 29-30).

Rine does not expressly teach the ethyl nicotinate having a log P value below 6.0. Rine does not expressly teach the composition comprising butyl benzoate.

Le et al. teaches the P value of ethyl niacin is 20.8. Therefore the Log P is equal to 1.32 (See page 15, Table 1).

Otsuka et al. teaches that butyl benzoate is useful as an adjuvant agent that indirectly promotes percutaneous absorption of the active in percutaneous application (See particularly col. 4, line 45-57).

It would have been obvious to one skill in the art when the invention was made to incorporate butyl benzoate into the method of Rine.

One of ordinary skill in the art would have motivated to incorporate butyl benzoate into the method of Rine because butyl benzoate is known to be useful as an adjuvant agent that indirectly promotes percutaneous absorption of the active agent. Therefore, incorporate butyl benzoate into the Rine composition would have been reasonably expected to increase the absorption of ethyl niacin and thereby increase the

hair treatment of Rine. The vasodilatation effect and thereby increasing the delivery of oxygen to tissue is inherent in the method of Rine.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abe et al. (US Patent 4,847,260) in view of Otsuka et al. (US Patent 5,151,271).

Abe et al. teaches a method of percutaneous delivery of an active by employing a composition comprises niacin esters including niacin octyl ester to increase the drug absorption (See particularly the abstract, col. 1, line 65 – 68, col. 3, line 28-29). Abe et al. also teaches that the niacin ester composition may be formulated into lotion (See particularly col. 6, line 14). Abe et al. teaches the weight percentage of nicotinic ester in the composition to be 0.5 to 70% (See col. 4, line 61).

Abe et al. does not expressly teach the percutaneous composition employed in the method contains butyl benzoate. Abe et al. does not expressly teach the weight percentage of the derivative of the vasodilator to be 0.05 to 5% or 0.1 to 1.0%.

Otsuka et al. teaches that butyl benzoate is useful as an adjuvant agent that indirectly promotes percutaneous absorption of the active in percutaneous application (See particularly col. 4, line 45-57).

It would have been obvious to one skill in the art when the invention was made to incorporate butyl benzoate into the percutaneous delivery method of Abe et al.

One of ordinary skill in the art would have motivated to incorporate butyl benzoate into the percutaneous delivery method of Abe et al. because butyl benzoate is known to be useful as an adjuvant agent that indirectly promotes percutaneous

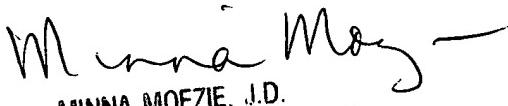
absorption of the active agent. Combining two or more agents which are known to be useful to increase the absorption of active individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069. Furthermore, the optimization of result effect parameters (e.g., weight percentage) is obvious as being within the skill of the artisan.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui  
December 28, 2001

  
MINNA MOEZIE, J.D.  
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